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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,750	03/31/2005	Hitoshi Arai	00005.001251	6890

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FITZPATRICK CELLA HARPER & SCINTO
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NEW YORK, NY 10112

EXAMINER

JAISLE, CECILIA M

ART UNIT	PAPER NUMBER
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1624

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/516,750

Applicant(s)

ARAI ET AL.

Examiner

Cecilia M. Jaisle

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 November 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 and 39-43 is/are pending in the application.
- 4a) Of the above claim(s) 3,6-9,16-27 and 39-43 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4,10-13,15 and 28 is/are rejected.
- 7) ☒ Claim(s) 5 and 14 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>31 March 2005</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Requirement for Information

Applicants and the assignee of this application are required under 37 CFR 1.105 to provide the following information that the examiner has determined is reasonably necessary to the examination of this application. If the compound excluded by the proviso in original claim 1, page 8, lines 14-17 after Formula (I) is known in the prior art, Applicants are required to submit such information for consideration by the examiner in regard to the patentability of the claims.

Restriction/Election

Applicants elected to prosecute the invention of Group I, Claims 1-27, drawn to bicyclic pyrimidine derivatives, and the species wherein $m=1$, $n=2$ and R^2 represents the moiety (ii) as defined in claim 1. Accordingly, claims 1, 2, 4, 5, 10-15 and 28 have been examined on their merits, to the extent that they are readable on the elected Group I and the elected species. To the extent that claim 1 is not readable on the elected Group I and the elected species, it is withdrawn. Claims 3, 6-9, 16-27 and 39-43 are withdrawn as directed to non-elected subject matter.

Rejection Under 35 USC 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

Art Unit: 1624

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4, 10-15 and 28 are rejected under 35 U.S.C. 112, paragraph one, because the specification, while being enabling for bicyclic pyrimidines represented by Formula (I), does not reasonably provide enablement for undefined derivatives thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Factors to be considered in making an enablement rejection are summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in the art, g) the predictability or unpredictability of the art and h) the breadth of the claims. *In re Colianni*, 195 USPQ 150 (CCPA 1977). *In re Rainer*, et al., 146 USPQ 218 (CCPA 1965). *Ex parte Formal*, 230 USPQ 546 (BPAI 1986).

- a) The term "derivative" may be interpreted as a residue or a different compound derived from the compounds of the claims, and is therefore confusing as to which compounds are envisaged as derived from the claimed compounds of formula (I). Because these claims are drawn specifically to compounds, deletion of the term "derivative" is suggested.

Art Unit: 1624

b) The specification merely mentions the Applicants' intention to make derivatives, without teaching the preparation thereof.

c) While the claims recite derivatives, no working examples show their formation. As stated in *Morton International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190, 1194

(Fed.Cir. 1993):

The specification purports to teach, with over fifty examples, the preparation of the claimed compounds ... However ... there is no evidence that such compounds exist ... [T]he examples ... do not produce the postulated compounds ... [T]here is ... no evidence that such compounds even exist.

The specification shows no evidence of the formation and existence of derivatives.

Applicants must show formation of derivatives or limit the claims accordingly.

d) The nature of the invention is chemical synthesis of derivatives, which involves chemical reactions.

e) The state of the art recognizes that the formation, composition and therapeutic activity of derivatives are unpredictable. The attached reference to Wikipedia shows that the term "derivative" refers to:

...a compound that is formed from a similar compound or a compound that can be imagined to arise from another compound, if one atom is replaced with another atom or group of atoms.

f) The artisan using Applicants' disclosure to prepare the claimed derivatives would be, e.g., an experienced process chemist with at least a BS chemistry degree.

Art Unit: 1624

- g) Chemical reactions are known as unpredictable. *In re Marzocchi, et al.*, 169 USPQ 367, 370 (CCPA 1971); *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970). See above regarding the unpredictability of derivative formation.
- h) The breadth of the claims includes thousands of compounds of Formula (I) 6, *inter alia*, as well as presently unknown compounds embraced by the word "derivative." See MPEP 2164.01(a), discussed *supra*, justifying the conclusion of lack of enablement commensurate with the claims. Undue experimentation will be required to practice Applicants' invention.

Deletion of the word "derivative" would overcome this rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4, 10-15 and 28 are rejected under 35 U.S.C. 112, paragraph two, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1, page 11, in the definition of R¹⁰, at the end of the first partial paragraph, the word --or-- should be inserted.

Rejection Under 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

Art Unit: 1624

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4, 10-13, 15 and 28 are rejected under 35 U.S.C. 102(b) as anticipated by U.S. 3,248,395, Ohnacker, issued April 26, 1966 (hereinafter, Ohnacker). See Examples 8, 9, 11-13, 16, 17, 20-22, 24, 25, 28, 29, 31, 33-35, 37-39, 41, 42, 44, 45, 48, 49, 54-58, 61, 63, 64, 66, 67, 69 and 70.

Rejection Under 35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Art Unit: 1624

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 2, 4, 10-13, 15 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ohnacker, describing (Examples 8, 9, 11-13, 16, 17, 20-22, 24, 25, 28, 29, 31, 33-35, 37-39, 41, 42, 44, 45, 48, 49, 54-58, 61, 63, 64, 66, 67, 69 and 70) 2-amino-4-amino-5,6,7,8-tetrahydro-pyrido-[4,3-d]-pyrimidines and their non-toxic, pharmacologically acceptable acid addition salts, exhibit antiphlogistic, antipyretic, diuretic, bacteriostatic, sedative and coronary dilating activities (col. 27, lines 22-28, *inter alia*). The presently claimed compounds encompass alkyl homologs and/or position isomers of the Ohnacker compounds, when, in the compounds of present Formula (I), R¹ is NR⁴R⁵, R² is Formula (II), A is a single bond, and R³ is hydrogen, alkyl or aryl, *inter alia*.

It would have been obvious to at the time the present invention was made to modify the Ohnacker compounds to prepare alkyl homologs and/or position isomers thereof. One of ordinary skill in the art would have been motivated to prepare the instantly claimed compounds because such structurally homologous and/or isomeric compounds are expected to possess similar properties to the Ohnacker compounds.

Art Unit: 1624

Compounds that are structurally homologous and/or isomeric to prior art compounds have been held to be *prima facie* obvious, absent a showing of unexpected results.

An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties.

In re Payne, 203 USPQ 245, 254 (CCPA 1979). See *In re Papesch*, 137 USPQ 43 (CCPA 1963) and *In re Dillon*, 16 USPQ2d 1897 (Fed.Cir. 1991) (discussed in MPEP § 2144) for an extensive case law review of obviousness based on close structural chemical compound similarity. See MPEP § 2144.08, ¶ II.A.4(c). Compounds which are homologs (compounds differing regularly by the successive addition or subtraction of the same chemical group, e.g., by -CH₃ or lower alkyl groups) or position isomers, as here, are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. *In re Wilder*, 195 USPQ 426 (CCPA 1977).

Allowable Subject Matter

Claims 5 and 14 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

The following is an examiner's statement of reasons for the indication of allowable subject matter. Claim 5 defines R⁵ as cycloalkyl and claim 14 defines R¹⁰ as NR^{8A}R^{9A}. These substituents are not taught or suggested by Ohnacker or by any of the other art of record.

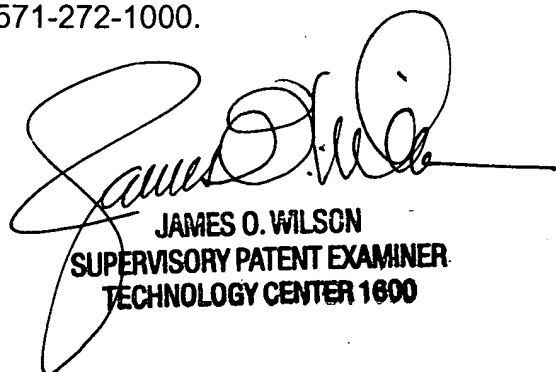
Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cecilia M. Jaisle, J.D. whose telephone number is 571-272-9931. The examiner can normally be reached on Monday through Friday; 8:30 am through 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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